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Cancer Epidemiology as Related to Chemicals in Drinking Water†

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Concern for the cancer risk posed by chemicals in drinking water stems in large part from advances in measurement techniques for environmental carcinogens. Recent recognition of the widespread occurrence in drinking water of chlorinated by-products of disinfection, as well as of organic solvents and other industrial chemicals, has stimulated many epidemiologic studies. Most have used population statistics to explore associations between geographic distributions of drinking water characteristics and cancer mortality rates. Others have compared water sources used by cancer victims with sources of persons dying from other diseases, relying on information from death certificates. Results from this first generation of studies point to associations between water quality and cancers of the colon, rectum, and urinary bladder. In the absence of direct environmental measures, most studies have used surrogate variables as indices of exposure. Among these variables are surface versus ground sources, chlorinated versus nonchlorinated water, and river water with upstream industrial discharges versus other sources.

We are collecting descriptive histories and analyzing finished drinking water samples from about 1000 public utilities as part of a large case-control interview study of bladder cancer. These data will permit a more comprehensive evaluation of the relationship between bladder cancer and water-borne carcinogens than has yet been possible and will answer many questions raised by the first studies. This study is described and earlier studies are reviewed from a perspective provided by our developing data base of environmental measurements.

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INTRODUCTION

Interdisciplinary communication between environmental epidemiologists and analytical chemists can stimulate thinking and research in areas of significance to both professions. This is especially true in the realm of water-borne contaminants, which are now under close scrutiny for their chemical characteristics and public health impact. Epidemiologists often rely on environmental survey measurements to identify exposed human populations. Conversely, the selection of geographic regions and environmental media for intensive chemical characterization is frequently guided by the appearance of unusual clusters of disease or mortality.

Assessment of potential health risks posed by organic contaminants in public water supplies is a challenging and difficult problem. The ultimate utility of such assessment is the incorporation of quantitative estimates of risk into well-informed environmental regulations. As the process of developing quantitative estimates continues, there are many observations along the way which contribute to a broad and growing base of environmental and health information. This review outlines some of the chemical and toxicologic evidence which give rise to concern, and then turns to illustrative examples from the epidemiologic literature. Exposure variables used in epidemiologic studies are evaluated in the context of water quality data recently gathered in conjunction with a large scale study of human bladder cancer.

ENVIRONMENTAL CHEMISTRY AND TOXICOLOGY BACKGROUND

Concern about organics in drinking water is largely due to major advances in environmental analytical chemistry brought about by the gas chromatograph and mass spectrometer. These devices lowered the limits of detection for many toxic chemicals by several orders of magnitude. They created a new awareness of the bewildering number and variety of chemical species in air and water to which human populations are exposed.

A list issued in 1974 by the U.S. Environmental Protection Agency (EPA) enumerated 187 organic compounds found in United States drinking waters. By 1979, the number had grown to more than 700.[1] There is little doubt that many more remain to be characterized, especially among the nonvolatile compounds.[2] Concentrates of organics from finished drinking waters are mutagenic in several *in vitro* systems.[3,4] Of the identified chemicals, at least 40 are known or suspect carcinogens, and three—vinyl chloride, benzene, and chloromethyl ether—have been

directly linked to human cancer.[5] Most of these chemicals appear in but a few supplies. In contrast, chloroform and other trihalomethanes (THM's)—bromodichloromethane, dibromochloromethane, and bromoform—are noted in almost every tested chlorinated supply[6–8] with chloroform levels ranging up to several hundred parts per billion.

In 1974, Rook[9] and Bellar and coworkers[10] independently demonstrated that THM's are formed during chlorination through interaction of chlorine, bromide ion, and organic precursors. Rook suggested that the precursors are largely humic acids, and showed experimentally that naturally occurring bromide could be oxidized by chlorine to the much more reactive free bromine. More recent work suggests that one half to two-thirds of organically bound chlorine is to be found in the higher molecular weight non-volatile fraction.[11] Chloroform is carcinogenic when fed to animals,[12,13] and the brominated THM's are mutagenic in bacterial testing systems.[14] Carcinogenicity of the brominated THM's, and indeed of hundreds of other chemicals found in drinking water, has not yet been evaluated.

For the purposes of epidemiologic studies, it is convenient to group organic contaminants into two broad categories, based on their origin either as industrial chemicals or products of chlorination. Industrial solvents, process intermediates and final products are found in receiving waters for industrial discharges and in wells drawing from contaminated aquifers. The THM's, especially chloroform, are noted in nearly all drinking waters disinfected with chlorine. Their concentration depends on precursor levels, chlorine dose, temperature, pH, and chlorine contact time.[15] The presence and concentration of bromide ion in the raw water source influences levels of the brominated species.

Mutagenicity tests can provide guidance in designing exposure categories in epidemiologic studies, since there is a strong correlation between mutagenesis *in vitro* and carcinogenesis *in vivo*.[16,17] Results from tests *in vitro* have been used in two ways to measure the toxicity of drinking water contaminants. Simmon and coworkers[14] have tested a number of individual compounds known to occur in potable waters. Other investigators have evaluated mixtures of organic concentrates from potable waters.[3,4,18] Three concentration methods have been used, singly and in combination: reverse osmosis, column chromatography (usually with an XAD resin), and freeze drying. Mutagenic concentrates are produced by each approach. The toxic potency of the sample is a function of water source, degree of concentration, and the mutagenicity assay system. Most volatile compounds are lost during the concentration step, so that a portion of the mutagenic (and therefore potentially carcinogenic compounds) in drinking water must reside in the higher molecular weight, nonvolatile fractions.

EPIDEMIOLOGIC STUDIES

Study strategies

At least 20 epidemiologic studies have assessed the relation between one or more aspects of water quality and one or more forms of cancer. The studies differ markedly in their designs and in what they can reveal about possible water–cancer relationships. Two comprehensive reviews of these studies have been prepared.[19,20]

One major distinction to be made among the epidemiologic studies is between geographic correlation and case-control studies. Geographic correlation (also called ecologic or aggregate) studies relate the rate of cancer in a group of individuals, e.g. within a town or a county, to the average or typical water exposure within that group. Case-control studies (a type of analytic or disaggregate study) relate one individual's risk of disease to his pattern of exposure.

The extent to which these investigations have actually examined the effects of organic contaminants in drinking water is a matter of some discussion. The lack of specific historical environmental data, especially chemical measurements, has compelled the use in epidemiologic studies of surrogate variables as somewhat crude measures of past exposure to waterborne organic chemicals. A later section of this paper evaluates this practice by looking at current chemical measurements in waters from different types of sources.

Several types of surrogate water quality indicators have been used. The proportion of a country's population using surface as opposed to ground water is one, and the county population served by chlorinated sources, in contrast to nonchlorinated, is another. The percentage of a county's population served by water from a river with upstream industry may be considered a special case of the surface/ground indicator. Other water quality variables used in epidemiologic studies have been trihalomethane concentration in the supply serving most of a county, and the historical chlorine dose in such supplies.

Geographic correlation studies

In 1973, the U.S. National Cancer Institute (NCI) published a compendium of cancer mortality rates for the years 1950–69, by anatomic site, for each of the 3056 counties of the contiguous United States.[21] These rates were presented separately for each race and sex and were adjusted for age. Two atlases, mapping the distribution of each type of cancer in whites and in nonwhites, respectively, were also issued.[22,23] These data have stimulated and facilitated several studies of water quality which use

regression models to explore the association between county water quality characteristics and site- and sex-specific cancer mortality rates. In most, a multiple regression equation is applied to adjust for county demographic and industrial characteristics known or thought to be related to the malignancy. The dependent variable in each of these models is a rate, specific for sex and race. This is expressed as a linear combination of several county characteristics, including a water quality variable. Calculated values of the regression coefficients reflect the relative contributions of the independent variables to the cancer rate.

The first three studies in Table I are examples of geographic correlation studies using county cancer mortality rates as the measure of health outcome. Page and coworkers addressed the issue of whether county (parish) populations in Louisiana served by the Mississippi had higher cancer rates than other groups.[24] The water variable in the regression model was the percent of a parish's population using Mississippi water, and it was included in the regression model along with several parish industrial and socioeconomic characteristics. The four race/sex groups were analyzed separately, and several grouped and individual anatomic sites were evaluated.

Salg examined data from the 346 counties in the Ohio River drainage.[25] All cancer sites were examined independently, using 1950–69 county cancer mortality data from NCI. The exposure index in one analysis was the percent of a county's population served by surface water and in another the percent with prechlorinated water. In addition to the water exposure variables, Salg included the following county-level variables in a multiple regression model: total population, population density, percentage non-white, median age, median educational level, median income, population change, percentage foreign stock, and two industrial variables. Each county cancer mortality rate, specific for sex and race, was regressed on the water exposure variable and the demographic and industrial variables.

The third study, by Cantor *et al.*, looked at cancer rates in counties with water supplies sampled by the United States Environmental Protection Agency in 1975.[26] The multivariate analysis was restricted to the 76 counties with more than 50% of their population served by the sampled supply. All cancer sites with rates greater than 1.5 per 100,000 population in white males and females were individually analyzed. The exposure in this case was a continuous variable, the total THM level, or, in separate analyses, the chloroform concentration or brominated THM level. Several demographic, socioeconomic, and industrial characteristics of the study counties were included in the regression model.

Correlational studies such as these have several advantages. They are

TABLE I

Representative epidemiologic studies of cancer and measures of water quality[a]

Investigator(s)	Study type	Exposure measures	Sex, race groups	Anatomic sites	Study location
Page *et al.* (24)	Geographic correlation	Percent parish using Mississippi water	WM, WF NM, NF	All combined urinary combined Gi combined	All Louisiana parishes
Salg (25)	Geographic correlation	1) % county drinking surface water 2) % county drinking pre-chlorinated water	WM, WF	All sites	346 counties in Ohio River drainage basin
Cantor *et al.* (26)	Geographic correlation	Trihalomethane concentration	WM, WF	All with rates 1,5/100,000/yr	76 counties across the U.S.
Alavanja *et al.* (27)	Case-control (mortality)	Chlorinated vs. non-chlorinated water	WM, WF NM, NF	Several GI sites Lung	Seven upstate NY counties
Brenniman *et al.* (28)	Case-control (mortality)	Chlorinated vs. non-chlorinated ground sites	WM, WF	GI and urinary sites	Illinois counties with ground water

[a]Abbreviations used: WM, white males; WF, white females; NM, nonwhite males; NF, nonwhite females; GI, gastrointestinal.

generally rapid, inexpensive, and use existing data sources. Their primary purpose is hypothesis generation; that is, a preliminary evaluation to determine if more detailed studies may be warranted. Inferences from correlational studies are limited because information on such potentially important factors as migration and historical exposure patterns is often incomplete or nonexistent. The measure of effect is the county cancer rate which is a group characteristic and not the particular experience of individual group members. Individuals who die of cancer may not be the most highly exposed members of the population. Information is often missing on other factors related to the risk of disease, such as cigarette smoking, and an observed association may be due to the confounding influence of these uncontrolled variables. Positive associations from such studies must therefore be interpreted with some caution since they may not reflect a cause-effect relationship.

The suspicion that a causal relationship may underlie statistical associations is increased, however, if several independent studies observe similar patterns of correlation in different regions, among different populations, and in both sexes.

Case-control studies

Case-control studies, in contrast to correlational studies, use information about individuals. The basic approach in these studies is to gather personal histories for persons with the disease of interest and for a series of matched individuals without the condition (controls). A comparison of the exposure status of cases and controls permits more specific estimates of risk than correlational studies. Case-control studies usually require more time and are more expensive than correlational studies. Their advantage lies in the stronger inferences which may be drawn and the greater precision of risk estimates. The most informative case-control studies employ interview data from newly diagnosed cases and their matched controls. Using the interview technique, one can collect detailed historical information on several exposures which may have influenced development of the disease. An alternate approach is to obtain information on cases and controls from systems of records such as death certificates.

The available case-control studies of water quality are based on analysis of mortality records of cancer deaths and of matched controls who died of other causes. They use residential information on the certificate of death, in conjunction with local water supply records, to establish characteristics of the drinking water supply at the person's last residence, and these in turn are used to estimate exposure.

The last two studies listed in Table I are representative case-control studies. Alavanja and coworkers contrasted the water source of cases who

died of one of several types of cancer, with sources of controls who died of other causes.[27] Decedents were drawn from seven countries in northern New York State. Cases consisted of all gastrointestinal cancers, all urinary tract cancer, and lung cancer. The risk factors related to water considered by Alavanja were chlorinated versus nonchlorinated water, and surface contrasted with ground water. The case-control approach allowed stratification by urban or rural residence of the decedent.

Brenniman used a similar approach in analyzing deaths from gastrointestinal and urinary tract cancers in parts of Illinois served by ground water sources.[28] The water quality variable was the chlorination status of the ground water source at the last residence of the decedent.

Case-control studies of cancer risk and water quality based on mortality records share some of the problems of correlational investigations. A change in residence, even 10 or 15 years before death, can result in misclassification of the water exposure variable because historical data which could provide water source information is not available on the death record. The period between exposure to carcinogens and appearance of a tumor is normally measured in decades, not years, so this type of error can be quite significant. Since no information is available for items such as cigarette smoking there is opportunity for confounding by such other risk factors. Despite these problems the available case control mortality studies represent a source of more specific information than the correlational studies. Case-control *interview* studies, in which current and historical information on a wide variety of factors is collected directly from patients and their matched controls, do not suffer from most of these drawbacks.

Results of epidemiologic studies

Results from available epidemiology studies will not be described here in detail. This information may be found in the two review articles mentioned above.[19,20] There is concensus among most observers that a clear cause-effect relationship of waterborne organics with human cancer has not been established by these studies, but that they do contain evidence suggestive of such links. In particular, cancers of the bladder, large intestine, and rectum are associated in many studies with one or another water quality variable. There is general agreement that these types of cancer are deserving of further evaluation in more highly focussed investigations, namely in case-control interview studies.[19,20,29,30]

AN ONGOING STUDY OF BLADDER CANCER

Suggested links between drinking water quality and bladder cancer are being pursued by incorporating a water quality component into a large

case-control interview study of bladder cancer. The investigation was originally motivated by the need for information on the human carcinogenicity of saccharin. The case-control design permitted, and indeed required, that information on other known and suspect causes of the disease also be gathered and considered in the analysis. In this study, we interviewed 3000 newly diagnosed cases which appeared during 1978 in ten areas of the United States, and a series of 6000 controls. By personal interview, we got information on demographic background, medical history, smoking history, occupational history, and history of artificial sweeteners use. Information on several other items such as coffee drinking habit, use of hair dyes, and fluid ingestion patterns was also gathered. A preliminary report on saccharin has been released.[31]

An historical water quality profile for each respondent is being created. We obtained a lifetime residential history from each participant and asked whether the primary drinking source at each residence was community, private well, bottled, or "other". For places and years where the respondent indicated a community source, we will use a data bank of historical information on community supplies in the ten study areas to obtain exposure information. This historical data bank of water quality will include 1000–1500 utilities serving more than 1000 persons. It covers the history of sources, treatments, and geographic areas served by each utility and also will contain chemical analyses of current samples. By linking this water supply information with personal residential histories, we will create a year-by-year water quality profile for each study participant.

MEASURES OF EXPOSURE IN EPIDEMIOLOGIC STUDIES

Several issues need resolution before we can decide on the optimal use of this large volume of environmental information. Table II summarizes a few of the epidemiologic approaches and types of historical and current data from which we can choose as we proceed with the analysis.

From an epidemiologic perspective, we will use several alternative methods for defining exposure dose and/or duration. Exposure can be defined as the *usual* type of water source as an adult; or whether the subject *ever used* a particular kind of source; or, to assess the length of time between exposure and tumor development (latent period), "years between first use of a suspect source and diagnosis of malignancy". Duration of exposure will be measured by the number of years that a person in our study used a suspect source.

The concepts "usually exposed as an adult", "ever exposed", "latent period", and "duration of exposure" are commonly used in epidemiologic

TABLE II

Measures and markers of dose in epidemiologic studies

Measures common to many studies	Measures specific to studies of water quality: Historical (and current) markers	Measures specific to studies of water quality: Chemical/toxicologic measurements (current only)
Ever exposed?	Surface (vs ground) souree	Trihalomethane (THM) level
Usual exposure as an adult	(Type of surface source;	Chloroform
Years since first exposure	protected, unprotected,	Brominated THM's
Number of years exposed	contains industrial	Total bound chlorine
	municipal effluent, etc.)	Chloroform
	Ground source aquifer	Brominated THM's
	Chlorinated (vs not)	Total bound chlorine
	Public (vs private) supply	Mutagenic potency
	Chlorine dose	

studies. "Exposures" in most studies are well-defined entities such as oral contraceptives, specific chemicals found in the workplace or unknown infectious agents. A central issue in studies of water quality and cancer concerns an acceptable and usable definition of "exposure" and "suspect source". Knowledge of the types of available historical information, combined with an informed judgment based on current data, can offer guidance in developing provisional answers to this question. The remainder of this paper is devoted to exploring this issue.

A principle underlying the discussion of exposures will be the importance of historical data. Most human cancers that have been linked to chemical or physical agents require decades to develop after first exposure to one or a combination of carcinogens. To establish links between environmental carcinogens and current disease it is therefore necessary to have knowledge of historical exposures to the carcinogenic substances in question.

Historical data for most water purveyors is of a qualitative nature. Past records from water resource agencies, health departments, or the utilities themselves describe sources of raw water (surface, ground, and characteristics of each), the types and locations of disinfection and other treatment practices, and the geographic areas served by utilities. It is less common that sources of historical data reveal quantitative information such as yearly average chlorine dose, although some large utilities maintain this type of information.

ENVIRONMENTAL CHEMISTRY AND EPIDEMIOLOGIC MEASURES OF EXPOSURE

To see if the available qualitative historical data on sources and treatments might be useful and adequate as exposure variables in epidemiologic studies, we have analyzed the first group of utility data collected. This information comes from a state in the midwestern United States with a population of about three million. Table III summarizes some characteristics of these data. We collected information and samples in this state from 289 sources used by 238 utilities. Of the 256 ground sources, 51 are not chlorinated, and these are found exclusively in small towns. Although surface sources represent 11% of the total number, they serve 23% of the population using community supplies. Another million people or so use very small community sources or their own private wells.

Ten volatile halocarbons in surface and ground sources

Table IV shows summary information from measurements of 10 volatile halocarbons in samples taken from each of the 238 chlorinated sources.

TABLE III

Source types and populations served (1979) for significant[a] community water supplies in a midwestern state

Type of source	Supplies		Service populations	
	Number	Percent	Number	Percent
Ground (not chlorinated)	51	17.7	96,000	5.1
Ground (chlorinated)	205	70.9	1,312,000	69.1
Surface (chlorinated)	33	11.4	443,000	23.3
Combined			46,000	2.5
	289	100.0	1,897,000	100.0

[a]Service population greater than 1000.

TABLE IV

Median level of halogenated compounds (mg/l) and CL_2 demand (mg/l) in 238 chlorinated water sources

Compound	Type of source		
	Ground		
	(Not alluvial) ($N = 129$)	(Alluvial) ($N = 76$)	Surface ($N = 33$)
Chloroform	0.6	1.8	107
Bromodichloromethane	0.1	2.2	32
Dibromochloromethane	0.1	3.0	2.2
Bromoform	"0"[a]	"0"	"0"
1,2-Dichloroethylene	"0"	"0"	"0"
1,1,1-Trichloroethane	"0"	"0"	"0"
Carbon tetrachloride	"0"	"0"	"0"
1,1,2-Trichloroethane	"0"	"0"	"0"
Tetrachloroethylene	"0"	0.1	"0"
1,2-Dichloroethane	"0"	"0"	"0"
Cl_2 added (mg/l)	1.9	1.8	9.1

[a]"0"—Below limit of detection (0.1 ppb for most compounds).

Sources are grouped as ground (non-alluvial aquifer), ground (alluvial aquifer), and surface. The median concentration of each of the 10 compounds is shown for each source type. The first four compounds listed are the THM's, and the remaining chemicals are probably of industrial origin. Median chloroform was 0.6 mg/liter in treated water from ground sources with non-alluvial (deep) aquifers, 1.8 mg/liter in ground-alluvial aquifer samples, and 107 mg/liter in samples from treated surface sources.

Bromodichloromethane shows the same general pattern across source types, but with lower concentrations. The concentration patterns of chloroform and bromodichloromethane result from major differences in raw water quality between surface and ground sources. Surface waters are generally much richer than ground sources in organic materials which react with chlorine to form chloroform. The median level of dibromochloromethane, in contrast, is highest in wells drawing from alluvial aquifers. This may result from higher bromide ion concentrations in these sources. Median levels of "industrial" compounds, except for tetrachloroethylene in alluvial aquifers, are below the one-tenth microgram per liter limit of detection. The last row in the Table IV shows median levels of the yearly average of added chlorine, in mg/liter. The median level in surface sources is 5 times that of ground sources. This points to the large difference between source types in the concentration of organics which can react with added chlorine.

TABLE V

Community water sources with high levels[a] of volatile halogenated hydrocarbons

	Predominant source type		Cutoff level for highest 5%
	Ground	Surface	
Chloroform	*	****	>110
Bromodichloromethane	*	****	>44.0
Dibromochloromethane	*****	—	>16.0
Bromoform	*****	—	>11.0
1,2-Dichloroethylene	****	*	>0.0
1,1,1-Trichloroethane	****	*	>0.8
Carbon tetrachloride	***	**	>0.0
1,1,2-Trichloroethane	****	*	>0.8
Tetrachloroethylene	****	*	>0.6
1,2-Dichloroethane	*****	—	>0.4

[a]Highest 5% of distribution of each compound.

Although median levels of most "industrial solvents" are below the detectable limit, these compounds are in fact observed in many supplies. The types of sources where the highest 5% of the distribution for each compound are found are shown in Table V. We expected to find elevated levels of these chemicals in surface sources, which often receive wastes from industrial processes, and it was surprising when the highest levels appeared in samples from ground sources. The high levels are possibly due to local contamination of aquifers by chemicals which have leached

from chemical waste disposal sites. Industrial solvents in some ground water sources of this state may well pose an important health risk to the exposed consumer populations but presence of such chemicals is probably not of major public health impact since relatively few people are served by these particular contaminated supplies. This does not necessarily minimize the importance of these contaminants in exposed populations, nor carry implications for other areas where contamination of ground sources is more widespread.

Products of chlorination such as halogenated nonvolatiles and the THM's might be of greater potential public health significance in this area of the United States, because of the size of exposed populations and the relative concentrations of contaminants.

Chloroform levels and chlorine dose

Figures 1 through 5 present data on chloroform levels and on chlorine dosage in the ground and surface sources. As discussed above, concentrations of chlorinated nonvolatiles tend to vary with chloroform levels,[32] so chloroform measures may be interpreted as representing a much larger class of compounds, many with demonstrated mutagenic and carcinogenic properties.

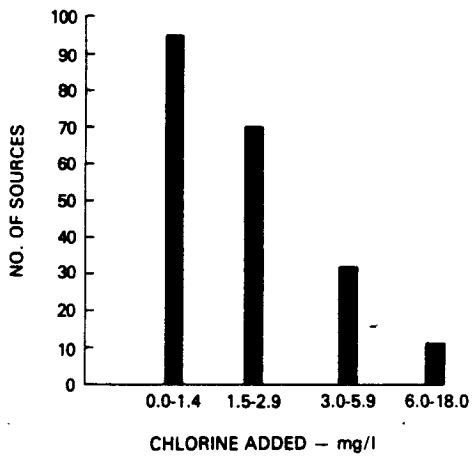


FIGURE 1 Distribution of annual average chlorine dose among 205 ground sources (1979).

Figure 1 shows how many ground sources had chlorine dosages in given ranges. It shows that most ground sources were treated with less than 3 mg/liter, with relatively few sources in the higher dose ranges.

Figure 2 shows the number of these same ground sources with

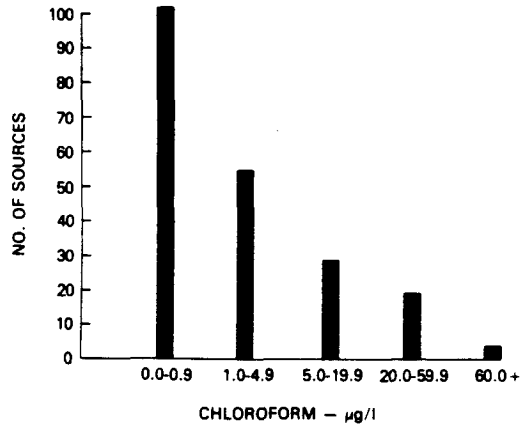


FIGURE 2 Distribution of measured chloroform levels in finished water from 205 chlorinated ground sources.

measured chloroform levels falling in different ranges. The distribution pattern of chloroform levels parallels the chlorine dosage pattern. Three-fourths of the samples from ground sources had chloroform levels less than 5 mg/liter.

Chlorine dosage and chloroform levels among surface sources contrast sharply with ground sources. Figure 3 shows how many surface sources had chlorine dosages of given levels. In contrast to ground sources (Figure 1), chlorine dose in most surface sources was greater than 6 mg/liter.

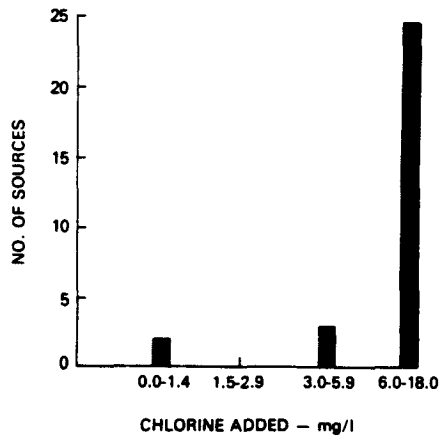


FIGURE 3 Distribution of annual average chlorine dose among 33 surface sources (1979).

Figure 4 shows chloroform levels among the surface sources. Again, in contrast to ground sources (Figure 2), surface sources tended to have higher chloroform concentrations, with most measuring above 60 mg/liter. Half of the 33 surface sources had chloroform levels greater than 107 mg/liter.

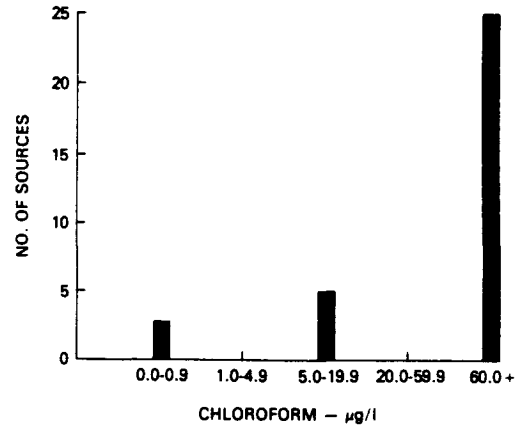


FIGURE 4 Distribution of measured chloroform levels in finished water from 33 chlorinated surface sources.

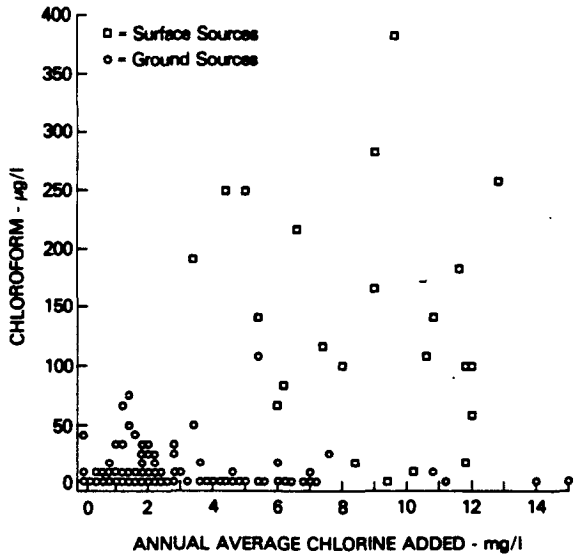


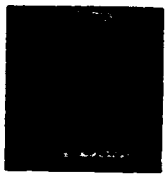
FIGURE 5 Measured chloroform levels versus chlorine dose in finished water from surface (□) and ground (○) sources. Many of the points represent 2 or more measurements.

Figure 5 shows the distribution of chloroform as a function of annual average chlorine added, in surface sources and in ground sources. Levels of both chloroform and of added chlorine are elevated in surface sources. Looking only within the surface or ground source categories, there is no within-group association of added chlorine with measured chloroform level. This counter-intuitive observation may result from the types of data we collected. "Chlorine added" is the reported average dose over the year prior to sampling, and chloroform was measured in a one-time grab sample in which the haloform reaction was allowed to go to completion. The lack of correlation between chlorine dose, and measured chloroform level, within source groups, implies that records of historical chlorine dose may not provide reliable and acceptable guides to levels of chlorination by-products in finished drinking waters. There are large differences in chlorine dose and in chloroform level (and presumably in levels of chlorinated non-volatiles) between ground and surface sources. Historical dosage information would, therefore, appear to provide no better guide to the mutagenic or carcinogenic potential of organics in finished drinking water than simple characterization of source type.

SUMMARY AND CONCLUSIONS

Our provisional conclusion on the best choice of exposure measures for epidemiologic studies is encouraging, in light of practices in completed studies, and the type of historical data possible to obtain. Surface sources contain the highest levels of chloroform, total trihalomethanes and presumably of halogenated nonvolatile compounds. In epidemiologic studies, persons served by surface sources should therefore be placed in a high exposure category. Nonchlorinated ground sources, although occasionally contaminated with industrial chemicals, are largely free of organics, and consumers of such water can be assumed to have the lowest exposures. At an intermediate level of exposure to water-borne organics are persons served by chlorinated ground sources. This group should perhaps be separated into persons using water from alluvial aquifers and those using water from other aquifers. In certain places with significant industrial development, special consideration should be given to contamination of ground and surface waters by man-made chemicals. In general, it appears that the exposure categories of most completed epidemiologic studies—surface versus ground, chlorinated as contrasted with nonchlorinated—are good choices. We will use these exposure categories in analysis of data from the large bladder cancer case-control study now nearing completion. By carefully examining historical drinking water exposures of individuals, we hope to provide a more precise answer

to the question of bladder cancer risk as related to drinking water quality than has yet been possible.



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